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EXAMINER	
STAPLES, MARK	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,505	LEXOW ET AL.	
	Examiner	Art Unit	
	Mark Staples	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02/29/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 17* is/are rejected.

7)☒ Claim(s) *8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/14/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of claims 1-12 of Group I in the reply filed on 12/29/2008 is acknowledged. Further acknowledgement is made of the amendments of claims 4-5, 7, 9, 11, and 12; submission of new claim 17; and cancellation of claims 13-16.

Claims 1-12 and 17 as filed on 12/29/2008 will be fully examined for patentability.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Great Britain on 16 April 2003. It is noted, however, that applicant has not filed a certified copy of the GB0308852.5 application as required by 35 U.S.C. 119(b).

Specification

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title should reflect that nucleotides are used to identify characteristics of molecules. The title should also be corrected to have the plural, "characteristics", as this is what is recited in the claims.

4. The use of the trademark TEXAS RED™ has been noted in this application. It and any other trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is advised to scan the entire application to ensure trademark usage in all the places where it appears in the application is in compliance with the current office guidelines.

Sequence Rules Compliance

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Applicant is given time of reply to this office action within which to comply with the sequence rules, 37 C.F.R. §§ 1.821-1.825. Failure to comply with these requirements will result in **abandonment** of the application under 37 C.F.R. § 1.821(g).

Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Pages 6 and 14 and Figures 1 and 3c respectively contain sequences without SEQ ID NOs. If these sequences are included in the sequence listing provide by Applicant, the specification should be amended to include the SEQ ID NOs. If these sequences were not included in the sequence listing filed 05/22/2007; Applicant should provide a substitute sequence listing and a CRF that include those sequences.

Claim Objections

6. Claim 8 is objected for recitation of ALEXA-RED and ALEXA-GREEN. They and any other trademarks should be capitalized wherever they appear.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

It is noted that these trademarks are be accompanied by the generic terminology.

Applicant is advised to scan the entire application to ensure trademark usage in all the places where it appears in the application is in compliance with the current office guidelines.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5, 7-12, and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying a series of characteristics which the sequence of a molecule which is a polynucleotide, does not reasonably provide enablement for identifying any series of characteristics of any molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

Claims 1-5, 7-12, and 17 are broadly drawn to methods of for identifying a series of characteristics of a molecule which encompasses all molecules including polynucleotides and every one of their components and properties including their functions. In fact the specification recites that the present invention provides both: 1) methods to identify binding characteristics of molecules, eg., protein binding properties, enzymatic properties or other chemical or biochemical properties (referred to hereafter as methods to identify chemical and biological properties and as recited in claims 1-5, 7-11, and 14), and 2) methods to identify characteristics which are sequences of molecules which are polynucleotides (referred to hereafter as methods to sequence polynucleotides as recited in instant claim 6). However, as will be further discussed, there is no support in the specification and prior art for the broadly claimed generic methods to identify chemical and biological properties, only support for the species methods to sequence polynucleotides. The invention is a class of invention which the Federal Circuit has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

The specification recites that if the molecule is a target polynucleotide the method may be used to determine the sequence of that target polynucleotide (see p. 6 lines 22-24). However, there is no evidence that characteristics of other molecules can be converted into a polynucleotide of defined sequence.

And there is a great deal of unpredictability of identifying characteristics of molecules. In an editorial overview Eckstein et al. (2002) present the following evidence

of this for the following molecules including characteristics of polynucleotides (nucleic acid biopolymers) of instant claim 5.

Proteins

"In any case, we can look forward to the production of proteins with hitherto unknown properties" (see p. 805, last sentence of the 2nd paragraph).

Short RNAs (in the section Nucleic-acid biopolymers, beginning on p. 805)

"Thus, there is no doubt that short RNAs have many surprises still in store and will remain the subject of exciting research for quite a while to come" (see p. 806, column 2, 4th sentence).

Carbohydrate biopolymers

"Hart and co-workers (pp 851–857) discuss O-linked GlcNAc transferase (OGT) and the possible cellular functions of O-GlcNAcylation, an important post-translational modification that is only beginning to be understood" (see p. 806, column 2, 1st sentence of 1st paragraph under the section heading).

"Hart and co-workers describe the need for better tools to analyze the proteins that are glycosylated by OGT as well as small molecules that can be used to specifically inhibit OGT to probe its function in various cell types and under various conditions" (see p. 807, the last sentence prior to the section *Peptide biopolymers).*

Peptide biopolymers

"However, as the number of three-dimensional structures of membrane proteins increases, we are beginning to obtain a ***glimpse*** of the features that stabilize membrane

protein structures and how these structures dictate their functions" (emphasis by Examiner, see p. 808, column 2, 2nd sentence).

The post filing date art further confirms the unpredictability of this area. Eckstein (2005) confirms that small RNAs still have properties of interactions and mechanisms which are unpredictable.

Small RNAs (short pieces of RNA)

"Given the multitude of interactions of the small noncoding RNAs revealed so far, we should be prepared to encounter, as yet, undiscovered interactions and mechanisms" (see last sentence of Abstract).

"There are many opportunities offered by the RNAi methodology; it is a challenging field with many unanswered questions, but with considerable potential in many areas" (see next to last sentence on p. 461, RNAi is inhibition of gene expression by small RNAs, see 1st sentence of Abstract).

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is a number of parameters which would have to be identified to apply this technology to any molecule. NIH (2001) reports that InfoChem has identified 4,000,000 small molecules. CAS Registry (2007) reports 59,895,306 known sequence molecules. Dr. Hurlbert (1999) teaches that: "Every molecule has certain unique chemical characteristics that differentiate it from all other molecules" (see middle of p. 3). Dr. Hurlbert further teaches that some of these characteristics are bonds which can be covalent or ionic, small atomic changes, hydrophobic associations, and hydrogen bonds. The instant claims recite methods to identify these other characteristics for any molecules of which millions

are known. The time table necessary to achieve a single generic method to identify a series of characteristics of any molecule would require a very large quantity of experimentation, if this were possible. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Working Examples

Other than for two examples of the specie methods of sequencing polynucleotides, the specification has no working examples of the generic methods to identify chemical and biological properties.

Guidance in the Specification.

The specification provides no evidence that the disclosed methods would be able to identify a series of characteristics in any molecule. The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention. The specification merely discloses methods for sequencing polynucleotides. Even if, arguendo, characteristics of any molecule could be coded by conversion into a polynucleotide; the characteristics must first be identified. There is no support on how the myriad characteristics of millions of molecules could be identified. The specification discloses that the series of characteristics which is the sequence of a target polynucleotide can be converted into another polynucleotide. However, a thorough review of the prior fails to show any enabled teachings of identifying a series of characteristics of any molecule and then converting those characteristics into a polynucleotide of defined sequence.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art identifying any characteristic of any molecules depends upon numerous known such as protein binding, enzymatic activity, three dimensional structure, post translational modifications, and even unknown properties the factor of unpredictability weighs heavily in favor of undue experimentation. Further, the prior art and the specification provides insufficient guidance to overcome the art recognized problems in all of these. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-5, 7-12, and 17 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. The term "characteristics of a molecule" in base claim 1 is an undefined term which renders the claim indefinite. The term "characteristics of a molecule" is not

defined by the claim, the specification does not provide a limiting definition, and as characteristics of a molecule can encompass myriads of components and properties of a molecule, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the claims (MPEP § 2171 requirement (B)). It is noted that the instant specification provides examples of characteristics of molecules (see 1st paragraph on p. 7), however no closed definition is given, and thus one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the claims. Dependent claims 2-5, 7-12, and 17 are thus also indefinite. It is further noted that while claim 5 limits the molecule to a target polynucleotide, the claim is indefinite as there are myriads of components and properties to a target polynucleotide including vast combinations of the type and number of component isotopes of the elements in the polynucleotide to the solubility properties of the polynucleotide in a plethora of different liquids. However, claim 6 is not indefinite as claim 6 does limit the characteristic to the partial or complete sequence of the target polynucleotide, the metes and bounds of which one of ordinary skill in the art would reasonably be apprised of.

12. Claim 4 recites the limitation "target" in line 2. There is insufficient antecedent basis for this limitation in the claim. Furthermore, the claim appears to be reciting that the targets are the units. However characteristics of the molecule (if this is the target) are converted into units. It is unclear how the "units" could even be targets. Claim 17, being dependent on claim 4, is likewise indefinite.

13. Claim 4 recites the limitation "same type" in line 2. There is insufficient antecedent basis for this limitation in the claim. It noted that the claim does not recite

the same bases; it is unclear what "type" means in the claim. Claim 17, being dependent on claim 4, is likewise indefinite.

14. Claim 17 recites the limitation "different type" in line 2. There is insufficient antecedent basis for this limitation in the claim. It noted that the claim does not recite a different base; it is unclear what "type" means in the claim.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1, 3, 5-7, and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Rosenthal et al. (WO 1993/21340, published 1993 and cited on the IDS), as evidenced by Bowden et al. (United States Patent H1,903 published October 3, 2000).

Regarding claims 1, 5, and 6, Rosenthal et al. teach methods for identifying a series of characteristics of a molecule (entire publication) comprising the steps of: (i) converting the characteristics of the molecule which is a RNA (a target polynucleotide) into a polynucleotide of defined sequence which is transcript cDNA, for sequencing, wherein each characteristic is represented by at least one distinct unit on the polynucleotide, the unit comprising at least a single base (see p. 1 lines 1-16 and see claim 1 step for forming a template), and Rosenthal et al. also teach converting a

desired/target nucleic acid fragment/polynucleotide into a single-stranded template/polynucleotide by generating the template from desired/target nucleic acid fragment/polynucleotide (see p. 7 lines 22-29);

(ii) contacting the polynucleotide with at least one of the nucleotides dATP, dTTP (dUTP), dGTP and dCTP, under conditions that permit the polymerisation reaction to proceed, wherein the at least one nucleotide comprises a detectable label specific for the nucleotide (see Scheme 1 beginning on p. 15 especially p. 15 lines 24-30 which are steps 1 and 2 and see p. 16 where the dNTP can be dATP, dTTP, dGTP, or dCTP, and see also claims 1-17 and 20);

(iii) removing any non-incorporated nucleotides and detecting any incorporation events by teaching removing excess reagents by washing and measuring the amount of incorporated label (see Scheme 1 beginning on p. 15; especially p. 15 lines 32-33 which are steps 3 and 4; and see also claims 1-17 and 20);

(iv) removing any labels (see Scheme 1 beginning on p. 15 especially p. 16 lines 1 which is step 6 as further explained on p. 16 lines 21-23 and see also claims 1-17 and 20); and

(v) repeating steps (ii) to (iv) to thereby identify the different units, and thereby the characteristics of the molecule (see Scheme 1 beginning on p. 15 especially p. 16 lines 15-17 which is step 11, and see also claims 1-17 and 20);.

Regarding claim 1, that RNA is converted to cDNA with at least a single base is further evidenced by Bowden et al. who teach reverse transcription:

> "The primer corresponding to the 3' portion of the RNA molecule (down stream primer) is used to convert RNA into cDNA in the presence of four types of deoxynucleoside triphosphates and reverse transcriptase" (see column 5 lines 49-52).

Regarding claim 3, Rosenthal et al. teach a method according to claim 1 or claim 2, wherein consecutive units on the polynucleotide have a different base type as the target for the incorporation of a labelled nucleotide by teaching where the first incorporated labeled nucleotide is dATP followed by incorporation of the next and inherently consecutive labeled nucleotide which is the different base of G in the labelled dGTP (see p 16 lines 19-29) where the bases incorporated are complementary to the polynucleotide template bases (see p. 9 lines 11-20).

Regarding claim 7, Rosenthal et al. teach wherein the labels can be fluorophores (see p. 3 lines 26-22).

Regarding claim 9, Rosenthal et al. teach wherein the polynucleotide template is bound, i.e. is immobilised, on a solid-phase support (see p. 7 lines 31-32).

Regarding claim 10, Rosenthal et al. teach wherein the immobilized/bound polynucleotide forms an array on the support material by teaching high resolution packaging of the template on an array (see p. 8 lines 31-37) and inherently teach that the array has a density which permits individual resolution of a detectable label by teaching all four labeled nucleotides used are detected (see p. 14 lines 18-24) and resolved, since the labels can be added until the resolving power of an apparatus is reached and then the removal or neutralisation of the labels is carried out in single step

reducing the number of label removal steps (see p. 14 lines 6-29) in the repeated labeling process (see for example p. 15 lines 6-9).

Regarding claim 11, Rosenthal et al. teach where detection is carried out by a fluorescence microscope (see for example p. 42 lines 24-26) which is a type of optical microscope.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 2, 4, 12, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenthal et al. as applied to claim 1 above, and further in view of Jones et al. (WO 2000/39333, published 2000 and cited on the IDS).

Rosenthal et al. teach as noted above.

Regarding claim 2, Rosenthal et al. do not specifically teach the limitations of a stop signal base.

Rosenthal et al. do not specifically teach the limitations of claims 4, 12, and 17.

Regarding claim 2, Jones et al. teach that along with converting characteristics of a target polynucleotide molecule into the coded polynucleotide that a stop base can be incorporated as specifically illustrated in Figure 7 where a stop "G" base has been incorporated for preventing ligation.

Regarding claims 4 and 17, Jones et al. teach wherein each unit comprises two bases of the same type as targets for the incorporation of labeled nucleotides by teaching where two or more bases on the target polynucleotide can be are associated with magnifying tag/units (see claims 1-3) and by teaching that magnifying tags and of target polynucleotide two base sequences can be two bases where the two bases include all permutations which are the 16 combinations of 4 bases including those two base (pairs) which are different (see p. 16 lines 24 and 25). Owing to the indefiniteness of claim 4 (see above), this claim has been interpreted as the "targets" being a part of the molecule, here the target polynucleotide. Jones et al. teach that a third base may be used as they teach more than one base may be used.

Regarding claim 12, Jones et al. teach wherein each of the bases A, T(U), G and C on the target polynucleotide is represented by a combination of two sequential units, with each base represented by a different combination of the two units; by teaching where each base on the target polynucleotide can be are associated with two or more magnifying tag/units (see claims 1-3) and by teaching that magnifying tags can be two bases where the two bases include all permutations which are the 16 combinations of 4 bases including those two base (pairs) which are different (see p. 16 lines 24 and 25).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods of Rosenthal et al. by using two bases instead of one base as suggested by Jones et al. with a reasonable expectation of success. The motivation to do so is provided by Jones et al. who teach that methods of coding characteristics of polynucleotide molecules is not limited to a one to one complementary conversion but can use multiple bases including two bases for coding one base and *vice versa* a single base for coding multiple bases including two bases (entire publication). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

20. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenthal et al. as applied to claims 1 and 7 above, and further in view of Rusinova et al. (2000).

Rosenthal et al. teach as noted above.

Regarding claim 8, Rosenthal et al. also teach where the label is fluorescein (see p. 11 line 27 to p. 12 line 5)

Rosenthal et al. do not specifically teach the limitations of claims 4, 12, and 17.

Regarding claim 8, Rusinova et al. teach ALEXA-GREEN (ALEXA-488, see Abstract) conjugated to biomolecules including nucleic acids and teach: "The Alexa and Oregon Green dyes are alternatives to fluorescein that offer additional useful properties".

Rosenthal et al. teach fluorescein can be a label in methods of identifying characteristics of polynucleotide molecules. Rosenthal et al. do not specifically teach ALEXA-GREEN. Rusinova et al. teach that the ALEXA-GREEN fluorescent label can be use to identify characteristics of polynucleotide molecules. Because both Rosenthal et al. and Rusinova et al. teach fluorescent labels to identify characteristics of polynucleotide molecules, it would have been obvious to one skilled in the art to substitute ALEXA-GREEN as taught by Rusinova et al. for the fluorescein taught by Rosenthal et al. in order to achieve the predictable result of identify characteristics of polynucleotide molecules using the ALEXA-GREEN fluorescent label. This is even more so as Rusinova et al. not only teach that ALEXA-GREEN can be substituted for fluoresecein, but that ALEXA-GREEN has useful properties which fluorescein does not have. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

21. No claim is free of the prior art.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 7:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples
/M. S./
Examiner, Art Unit 1637
June 18, 2008

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637